

### **REMARKS**

Claims 19 and 28 are currently pending in the present application. Claim 19 is the only independent claim.

Claims 23-27, 32-34, and 37 have been cancelled without disclaimer or prejudice to their inclusion in one or more related applications.

### **Explanation of the Amendments**

The title has been changed to reflect the claims, as suggested by the Examiner, and now reads as "A TRANSGENIC MAMMAL SECRETING B-DOMAIN DELETED HUMAN FVIII IN ITS MILK".

For clarity, without prejudice or disclaimer, claims 19 and 28 have been amended, among other ways to incorporate into them the full SEQ ID NO:15 from claim 24, which the Examiner indicated at page 11, lines 8-9 of the Office Action was free of the prior art. The amendments are otherwise supported by the original specification and claims, as noted in previous responses.

Since the amendments made herein introduce no new matter, entry of the amendments is proper and respectfully requested.

### **Claim Rejections Under 35 U.S.C. § 112**

Claims 19 and 23-31 are rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement, because the previously amended claims introduced new matter.

Without acquiescing to the Examiner's reasoning, the insertion in the Prior Amendment of the species of a B-domain deleted human clotting factor VIII polypeptide having amino acid residues 18 to 1448 of SEQ ID NO:15 has been deleted in the remaining claims 19 and 28. B-domain deleted human clotting factor VIII polypeptide having the amino acid sequence of the full-length SEQ ID NO:15 is recited, as set forth at page 19, lines 3-4 of the application as filed.

### **Claim Rejections for Obviousness**

The Examiner has rejected claims 19 and 25-28 under 35 U.S.C. § 103(a) as being obvious over Chen (*Transgenic Research*, 11:257-268, 2002) ("Chen"), in view of Soukharev

(*Blood Cells, Molecules and Diseases*, 28:234-248, 2002) (“Soukharev”) and Jolly (WO 98/00541) (“Jolly”), and supported by Lubon (US Patent 6,255,554) (“Lubon”).

Applicants respectfully submit that amended claims 19 and 28 are not obvious in view of the cited prior art references, alone or in combination, at least because the references do not teach or suggest a transgenic mammal that releases B-domain deleted rFVIII in milk, and the B-domain deleted rFVIII polypeptide has the amino acid sequence of SEQ ID NO:15. The Examiner recognized that the prior art does not anticipate or render obvious the polypeptide having the amino acid sequence of SEQ ID NO:15, as noted above.

The present BDD-rFVIII has a deletion of the B domain between Ser 741 and Leu 1643 of the full human Factor VIII sequence. Although Jolly discussed numerous B-domain deleted hFVIII known in the art for use in genetic engineering (pages 25-28), none of those disclosed the same spliced site as described in the present invention. Even though Jolly suggested a specific B domain deletion called the SQN deletion, which deleted the amino acid residues 744 to 1637 from the B domain creating a Ser-Glu-Asn (SQN) link between the A2 and A3 FVIII domains (see page 25, lines 23-30, and page 26, lines 1-5), the deleted residues 744 to 1637 are different from those as provided in the B-domain deletion site being Ser 741 to Leu 1643, rather than following the SQN deletion.

As discussed above, in view of the prior art teaching, one of ordinary skill in the art would not have been motivated to make the B-domain deleted rFVIII recited in the present claims that has the deletion of the B domain between Ser 741 and Leu 1643, thus the particular fusion junction of Ser 741-Leu 1643. One of ordinary skill in the art would not know to make a non-human transgenic mammal having a genome with a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:15, which secretes the B-domain deleted human FVIII polypeptide in milk.

Reconsideration and withdrawal of the rejections are respectfully requested.

Applicants respectfully submit that claims 19 and 28 are in condition for allowance.

Applicants appreciate the effort of the Examiner and look forward to receiving Notice of Allowance of all pending claims.

Respectfully submitted,

**WINSTON T.K. CHENG *et al.***

Sept. 18, 2009  
(Date)

By:



**ALAN S. NADEL**

Registration No. 27,363

**PANITCH SCHWARZE BELISARIO & NADEL LLP**

One Commerce Square

2005 Market Street, Suite 2200

Philadelphia, PA 19103-7013

Telephone: 215-965-1330

**Direct Dial: 215-965-1280**

Facsimile: 215-965-1331

E-Mail: [anadel@panitchlaw.com](mailto:anadel@panitchlaw.com)

ASN